UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,802	03/23/2005	Greta Van Der Berghe	BERGHE1	6222

1444 7590 05/01/2008

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
05/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,802	VAN DER BERGHE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-67 and 71-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-67 and 71-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 02/20/2008, is acknowledged.

2. Claims 51, 54-58, 51-67, 71-85 are pending and under examination in the instant application.

3. The recitation "consists essentially only of MBL protein oligmers" in claims 84-85 is objected to because it is not clear what the term "consists essentially only of" encompasses.

4. The issue of unity is moot since the Examiner now is addressing on all pending claims.

5. In view of the amendment filed on 2/20/08, only the following rejections are remained.

6. The rejection under 35 U.S.C. 102(e) as being anticipated by US 20050037949A1 is hereby withdrawn because no benefit of the filing date of the foreign application is given under 102(e) (1).

7. The rejection under 35 U.S.C. 103(a) as being unpatentable over US 20050037949A1 in view of US. Pat. No. 6,245,334 is hereby withdrawn because no benefit of the filing date of the foreign application is given under 102(e) (1).

8. Claims 51, 54-58, 51-67, 71-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in the previous Office Action mailed 8/23/07.

Applicant's arguments, filed 2/20/08, have been fully considered, but have not been found convincing.

Applicant submits that they are not obligated to disclose the sequence of every naturally occurring form (allelic variant) of human MBL.

The Examiner agrees with applicant statement, however, at issue is that the specification fails to disclose which of these MBL allelic variants "one or more" is important to reduce the risk of infection associated with an organ transplantation. Accordingly, the skilled in the art would not know which of the claimed "one or more of MBL proteins" can be administered in the claimed method of reducing the risk of infection associated with an organ transplantation. There is no nexus between the MBL allelic variants and the claimed reduction of the risk of infection associated with an organ transplantation.

Applicant argues regarding "any organ" that it should be understood that the MBL is not administered to reduce the risk of rejection of the transplant. Rather, it is principal purpose is to reduce the risk of subsequent infection. Applicant points to Ginns et al., Organ Transplantation (1999) support the contention that organ transplantation is a mature technology.

However, Applicant is claiming a method of reducing the risk of infection associated with an organ transplantation and not organ transplantation. Pizzo (The new England Journal of Medicine, 1999) teaches several major risk factors associated with solid organ transplantation such as the site of transplantation, underlying disease and prior infection status, status of underlying disease, nutritional status, age, immunosuprressive regimen which cause the alterations in host defense that increase the risk of infection. Applicant did not address these factors in relation to infection associated organ transplantations. Applicant did not address the incidence of infection in these transplant recipients.

Regarding Dahl (2004), Applicant points to Dahl's teachings "MBL deficiency may only come into play when other parts of the immune system are compromised, e.g. by chemotherapy .... MBL deficiency has been associated with increased risk for severe and recurrent infections, but almost solely in hospital studies". Applicant concludes that the instant invention relates to management of critically ill patients for whom "hospital studies" would be relevant.

However, Applicant's own specification on page 3, lines 26-29 discloses that the present invention demonstrated for the first time an efficient MBL therapy for critically ill patients in the ICU, which were not previously been immunocompromised (e.g. not immunosu- pressed after organ transplantation or by disease).

Regarding Berger (2005 and 2007) Applicants admit that they don't know whether the same rejection pattern would be seen in MBL-deficient individuals receiving MBL replacement therapy. Applicants made no comment regarding US 2004/0259771 teachings.

However, *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicant concludes that it does not appear that the Examiner has conclusively demonstrated that MBL would have an adverse effect on graft or patient survival after renal (or pancreatic) transplantation. Even if it did, it might still provide net benefits for some transplant patients, e.g., liver transplant patients.

Contrary to Applicant assertions Berger (2005 and 2007) teachings demonstrated that MBL would have an adverse effect on graft or patient survival after renal or pancreatic transplantation. Applicant did not elucidate the underling pathophysiological mechanisms to reduce the risk of infection in such renal or pancreatic transplantations using the claim human MBL protein.

Applicant points to the declarations under 37 CFR 1.132 by Dr. Alison Freifeld, filed 2/20/08 to support of the claimed efficacy of MBL in a transplantation context, Freifeld Declaration I presents preliminary results from an ongoing liver transplant study. The pharmacodynamic response of MBL administration is measured as the rise in C4 complement concentration. These data show that administration of rhMBL normalizes complement C4b deposition (a marker for activation of the MBLectin complement pathway) and that C4b deposition correlates with rhMBL levels.

However, Dr. Freifeld declaration filed 2/20/08 under 37 CFR 1.132 does not commensurate with the scope of the claimed invention. Accordingly, the declaration is insufficient to overcome the rejection of record. The declaration is limited to liver transplantations and says nothing, for example, about renal or pancreatic transplantations. Moreover, the data presented says nothing about reducing the risk of infection associated with an organ transplantation, but rather evaluate the safety and tolerabaility of IV recombinant rhMBL in liver transplant recipients. The data presented does not look at the incidence of infection in these transplant recipients. The data presented provide a correlation between the plasma concentration of MBL and the concentration of complement C4b, wherein administration of rhMBL to liver transplant recipients increases complement activity. While, the declaration states that the complement system is an important part of the innate immune response and thus important for the protection against infections, the declaration presents no data to support the statement. The skill in the art would not know whether the administration of rhMBL would reduce the incidence of infection in these transplant recipients. The Declaration states that administration of rhMBL to liver transplant patients did not result in organ rejection in any of the patients who had received it. However, no control data to compare patients without administering rhMBL on the liver transplant patients.

Regarding Dr. Freifeld decaration II, the examiner notes that Dr. Freifeld did not review and understood the Office communication of 8/23/07, by inserting the phrase "not yet". It appears that the declaration is directed to distinguish the solid organ transplantations and bone marrow or hematopoietic cell transplantations under the obviousness art rejection and not for the enablement rejection.

9. The following new ground of rejections are necessitated by the amendment submitted 2/20/08.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 51, 54-58, 51-67, 71-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullighan et al (Blood 99(10):3524-3529, May2002, of record) in view of Pizzo (1999).

Mullighan *et al* teach that MBL gene polymorphisms are associated with major infection following allogeneic hemopoietic stem cell transplantation (SCT). Mullighan et al teach that MBL2 genotype influences the risk of infection following allogeneic SCT and that both donor and recipient MBL2 genotype are important. Mulligan et al also teach that these findings raise the possibility that MBL replacement therapy may be useful following transplantation (see abstract). Mullighan et al teach that there is considerable interest in the role of purified or recombinant MBL as a potential therapeutic agent. Early data suggest that administration of purified MBL is safe and may be effective in ameliorating infection frequency in MBL-deficient individuals. Intensive antimicrobial treatment for infection after SCT is often toxic or unsuccessful, and existing strategies to prevent infection such as prophylactic antimicrobials and intravenous immunoglobulin (which contains non MBL) are incompletely effective. Further, if MBL deficiency is confirmed by future genetic and functional studies to be a major risk factor for infection after SCT, this clinical setting would be an ideal scenario for a clinical trial of MBL replacement therapy (see page 3529 last ¶ in particular). In addition, Mullighan et al teach that life-threatening complications such as GVHD and infection remain major barriers to the success of allogenenic hemopoietic SCT. While pretransplantation conditioning and posttransplantation immunosuppression are important risk factors for infection, the reasons that similarly immunosuppressed transplant recipients show marked variation in frequency of infection after allogeneic SCT are unclear. MBL deficiency is a risk factor for infection in other situations where immunity is compromised (see abstract).

Mullighan's *et al* teaching differs from the claimed invention in the recitation of organ transplantation.

Pizzo teaches that both BMT and solid organ transplantation are initially like high-risk patients with infection, the only difference is that the increased risk of bacterial infections is during late post-transplantation period in BMT, while in solid-organ transplants the increased risk of bacterial infections during the first few weeks after transplantation (see page 897, 1st col., top ¶ in partiuclar). The risk of infections is heightened by certain immunosuppressive agents (e.g., cyclosporine) that are given after solid-organ transplantation (see page 895, 1st col., 2nd full ¶). Solid organ transplantation can be immunocompromised at the site of the transplant (see table I). Patients who have neutropenia after cytotoxic chemotherapy or immediately after preparative therapy for transplantation nearly always have breaches of physical defense barriers, typically with oral and gastrointestinal mucositis, which permit changes in colonization as well as serving

as nidi for local infection and entry points for systemic invasion. Such patients are also likely to have alterations in cellular immunity which make these patients among the most vulnerable to acute infections (see the ¶ bridging pages 893-894). Finally, Pizzo teaches that the guiding principle has been to treat severely immunocompromised, febrile patients empirically for the major pathogens to which they are vulnerable at the particular period of their immunosuppression (e.g., immediately after chemotherapy as compared with weeks or months after bone marrow or solid-organ transplantation). Broad-spectrum antibiotic therapy is administered to cover gram-positive and gram-negative aerobic organisms. Either combination antibiotic regimens or monotherapy with selected third-generation cephalosporins or carbapenems is used. The specific approach varies according to the type of immunocompromise (Table 4). The proportion of immunocompromised patients treated outside the hospital is increasing (see 899, 1st col., 1st full ¶ in particular).

However, it would be conventional and within the skill of the art to easily adapt the mullighan's et al teachings to an in vivo model of organ transplantation. It would be obvious to administer the MBL replacement therapy for the immunosuppression drugs. It would be conventional-and within the preview of those skilled in the art to identify and determine the optimum treatment protocols to reduce the risk of infection in organ transplantations. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because an organ transplant is immunocompromised from the use of agents that depress one or more components of the immune system which increases the risk of an infectious complication as taught by Pizzo.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 2/20/08, have been fully considered, but have not been found convincing.

Applicant submits that clam 51 is amended to specify organ transplantation. Applicant submits that transplantation of organs is distinctly different from transplantation of stem cells, as explained in the attached Freifeld Declaration II.

While transplantation of organs may be distinctly different from transplantation of stem cells as stated in the Dr. Freifeld declaration II, however, the risk of infection is not distinctly different in

said transplantations in view of Pizzo teachings. While Dr. Freifeld declaration under 37 C.F.R. 1.132 filed 2/20/08 states that solid organ transplantations and bone marrow or hematopoietic cell transplantations are distinct scenarios, which raise different difficulties. It is not obvious to adapt teachings from one type to the other due to the differences. The Examiner's position is that obviousness is a legal determination and is not a scientific determination. Declarant is not in a position to make such determination. Moreover, Declarant states that she did not yet review and understood the Office Communication of August, 23, 2007 but yet made that determination.

12. Claims 51, 54-58, 51-67, 71-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/69894 in view of PIZZO (1999).

The `894 publication teaches and claims the use of a composition comprising at least one mannan-binding lectin (MBL) sub-unit, or at least one mannan-binding lectin (MBL) oligomer comprising the at least one mannan-binding lectin (MBL) subunit, in the manufacture of a medicament for prophylaxis and/or treatment of infection in an individual being classifiable as: a) an individual having an immunocompromised condition; and/or b) an individual being at risk of acquiring an immunocompromised condition resulting from a medical treatment; and/or c) an individual having a serum level of MBL in excess of 50 ng/ml serum (see published claim 1 in particular), wherein said oligomer is preferably selected from the group of oligomers consisting of tetramers, pentamers and/or hexamers (see published claim 3 in particular), wherein said immunocompromised condition is neutropenia (see published claim 7), wherein the infection is an infection caused by a microbial species (see published claim 9), such as a fungus, a yest or a bacteria (see published claims 10-12), wherein the bacteria species is a pathogenic (see published claim 15), wherein the MBL is a human MBL subunit (see published claim 31), wherein the medicament is administered to the individual prior to another treatment resulting in an immunocompromising condition in the individual (see published claim 32), wherein the medicament is administered to the individual simultaneously, sequentially or separately with a medical treatment, said medical treatment resulting in an immunocompromising condition in the individual (see published claim 33), wherein the medicament is administered to the individual prior to, during and after said medical treatment (see published claim 34), wherein the treatment is a prophylactic " treatment (see published claim 36), said medical treatment is chemotherapy (see published claim 36). Finally, the `894 publication teaches that all individuals being immuno-compromised or at risk of becoming immuno-compromised should be treated with MBL independent of their specific MBL level (see page 7, lines 31-33 in particular).

The claimed invention differs from the reference teachings only by the recitation the immunocompromised condition is characterized by infection associated with an organ transplantation in base claim 51 or adverse condition associated with an organ transplantation in claim 74.

Pizzo teaches that the the risk of infections is heightened by certain immunosuppressive agents (e.g., cyclosporine) that are given after solid-organ transplantation (see page 895, 1st col., 2nd full ¶). Solid organ transplantation can be immunocompromised at the site of the transplant (see table I). Patients who have neutropenia after cytotoxic chemotherapy or immediately after preparative therapy for transplantation nearly always have breaches of physical defense barriers, typically with oral and gastrointestinal mucositis, which permit changes in colonization as well as serving as nidi for local infection and entry points for systemic invasion. Such patients are also likely to have alterations in cellular immunity which make these patients among the most vulnerable to acute infections (see the ¶ bridging pages 893-894). Finally, Pizzo teaches that The guiding principle has been to treat severely immunocompromised, febrile patients empirically for the major pathogens to which they are vulnerable at the particular period of their immunosuppression (e.g., immediately after chemotherapy as compared with weeks or months after bone marrow or solid-organ transplantation). Broad-spectrum antibiotic therapy is administered to cover gram-positive and gram-negative aerobic organisms. Either combination antibiotic regimens or monotherapy with selected third-generation cephalosporins or carbapenems is used. The specific approach varies according to the type of immunocompromise (Table 4). The proportion of immunocompromised patients treated outside the hospital is increasing (see 899, 1st col., 1st full ¶ in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer human MBL protein taught by the 894 publication to an infection associated with an organ transplantaton taught by Pizzo.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because an organ transplant is immunocompromised from the use of agents that depress one or more components of the immune system which increases the risk of an infectious complication as taught by Pizzo.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claims 51, 54-58, 51-67, 71-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrases:

A. “at least one adverse condition" claimed in claim 74,

B. "one or more human MBL proteins which may be the same or different, said human MBL proteins comprising one or more human MBL protein monomers of about 96kDa, each monomer consisting of three identical human MBL polypeptide chains, each chain of about 32 kd" claimed in claims 51 and 74,

C. "may be the same or different, and are independently selected from the group of oligmers consisting of trimers, tetramers, pentamers and hexamers of said about 96kDa MBL protein monomer" in claims 61 and 81,

D. "a mannan-binding lectin (MBL) protein of about 96 kDa, consisting of a single MBL protein monomer, said monomer consisting of three identical about 32 kDa MbL polypeptide chains", in claim 62,

E. "a plurality of mannan-binding lectin (MBL) protein monomers, each of about 96 kDa, each monomer consisting of three identical about 32 kDa MBL polypeptide chains", in claims 63 and 80,

F. "infection subsequent to the organ transplantation" in claim 75,

G. " MBL consists essentially only of MBL protein oligomers, each oligomer consisting of two or more MBL 96 kDa protein monomers" in claim 84,

H. "MBL consists essentially only of MBL protein oligomers, each oligomer consistingof two or more MBL 96 kDa protein monomers", in claim 85,

represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 2/20/08 points to the specification at page 6, lines 25-30, page 18, line 26, page 19, line 24 and page 24, lines 14-15, for support for the newly added limitations as claimed in claims 51, 54-58, 51-67, 71-85. However, the specification does not provide a clear support for such limitations. For example, the examiner was unable to find support for the subgenus "at least one adverse condition", however, Applicant is creating a new genus of transplantation which was not contemplated in the specification and claims. A subgenus is not necessarily implicitly described by a genus encompassing it and a species upon which it reads, see *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972).

Another Example, the "may be the same or different", "independently" or "plurality" nothing in the specification point to mix and match, selection between oligomers or administering one or more human MBL protein.

The Examiner cannot see the relationship between the 96kDa polypeptide chains in the WO0070043 and the instant application. Further, the incorporation of essential material in the specification by reference to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be

accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

It is noted that obviousness is not the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). It is requested that Applicant maps each claim limitation to the instant specification and claims as originally filed in response to this office action. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 51, 54-58, 51-67 and 71-85 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/70043.

The WO `043 publication teaches a method of use of MBL or fragment thereof in a pharmaceutical composition for the treatment comprising cure (administration after and during) and/or prophylaxis (administration prior to) of conditions of diseases and disorders in need of treatment, wherein said diseases, disorders and/or conditions are infections in connection with implantation and/or transplantation of organs (see page 12, last ¶ to page 13 1st ¶ and page 25, lines 16-28 in particular). The rMBL is used to enhance the ability of the immune defense to recognise and kill microbial pathogens (see page 27, lines 24-29). The `043 publication teaches that MBL form which is similar to natural human MBL or a recombinant human MBL comprising oligomers of MBL which refers to the various "mers" of MBL, such as monomer, dimer, trimer, tetramer, pentamer and hexamer. The monomer consists of three identical peptide chains. The other oligmers are formed as combiation of 2-6subunits. (see page 10, lines 1-12). The `043 publication teaches that the human MBL protein is composed of up to 18 identical 32 kDa polypeptide chains (see page 2, lines 15-22 in particular). The `043 publication teaches that the treatment is a treatmetn of a condition of deficiency of MBL (pre determined minimum MBL polypeptide serum level) (see page 25, lines 14-15). Further, the observed low plasma concentrations of MBL (below 500 ng/ml) are indicative for an increased susceptibility to clinical significant infections and the immune defense of these patients can be reinforced by administration of recombinant or natural plasma-derived MBL (see page 26, L30-33 in particular). The `043 publication teaches treating allogenic bone marrow transplantation (BTM) with claim MBL polypeptides (see page 26, line 13 in particular).

Claim 54 included because infection in connection with organ transplantation by definition means a patient who is being operated and where complications supervene.

Claim 55-56 is included because it is readily apparent that infection associated with an organ transplantation is a life threatening condition, and requires ICU administration of the MBL. The "increase survival rate" and reduce the time that a patient stays within the hospital" are inherent to the claimed method. In addition, the claimed invention is a single step method, and `043 publication teaches the claimed step method of reducing the risk of infection associated with an organ transplantation with MBL protein.

Claims 57-58 are included because "treatment" of infection in connection with organ transplantation in a patient is a patient suffers from "post-surgical critical illness" and "post-traumatic critical illness".

Claims 65- 67 are included because the `043 patent teaches that normally form 1-100 mg is administered per dosage, such as from 2-10mg, mostly from 5-10 mg per dosage. Mostly about 0.1 mg/kg body weight is administered. Such dosages would result in a blood level above 500 ng/ml or 1000 ng/ml or between 1000-2000 ng/ml in the patient in the absence of evidence to the contrary.

The recitations "hence by reducing the risk of infection the MBL reduces the risk of SIRS" in claim 73; "reduced the risk of a fatal outcome" in claims 72 and 82 are inherent property to the referenced method of treatment comprising cure and/or prophylaxis of conditions of diseases and disorders in need of treatment, wherein said diseases, disorders and/or conditions are infections in connection with transplantation of organs with MBL protein.

The reference teachings anticipates that claimed invention.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 29, 2008

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644